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THE BRITISH JOURNAL OF DERMATOLOGY

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THE BRITISH
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SEPTEMBER, 1911.

ICHTHYOSIS HYSTRIX AND NÆVUS VERRUCOSUS.

By J. L. BUNCH, M.D., D.Sc.,
Physician to the Skin-Department, Queen's Hospital for Children, London.

The question of the origin of nævi has always been a vexed question, and has not yet been finally decided any more than the relation of certain varieties of nævus to certain forms of ichthyosis. The supporters of the epithelial origin of nævi still assert that in sections of nævi they can see cells which can only be of epithelial origin, although situated in the corium, and that these cells have probably grown down from the epithelium into the true skin, losing their cell-fibrillation and acquiring other characteristics in the process. Schütz and others, however, entirely deny that there are transition stages between epithelial and nævoid cells, and assert that such appearances are brought about by cutting the sections obliquely, by pressure, and by slight œdema of the cells. They declare that the cells are embryonic connective cells which have been arrested in their development on their way to form true fixed connective tissue, and their derivatives have similar imperfect powers of being transformed into elastic tissue or connective tissue. The development of pigment is probably not an acquired function of nævus cells at all, but the pigment is derived from adjacent melanoblasts, whose processes make their way into the cells and deposit pigment there.

To bridge over these two directly conflicting views is a matter of extreme difficulty, inasmuch as the alterations which can take place in an epithelial cell which has grown down into the corium are but imperfectly defined, and such appearances might of course also be

simulated by embryonic connective-tissue cells during certain stages of their growth.

The fact that some of these nævi may undergo certain degenerative changes, and, as in the case here dealt with, take on a sarcomatous development, is in my opinion in favour of their origin from embryonic connective-tissue cells. A further argument in support of this theory is the tendency (if this be indeed the case) for linear nævi to follow the course of the embryonic sutures rather than the lines of cleavage, the course of the blood-vessels or the distribution of cutaneous nerves.

The case was as follows: A youth, aged 22 years, had had a well-marked Nævus verrucosus covering the anterior surface of one knee as long as he could remember (Fig. 1). The skin over the patella and above and below this was when seen thickened, hard and irregular on the surface with deep furrows, but no raised warty growths. The verrucose thickening did not seem to impede the movements of the knee appreciably. The patient said that the lesions had not increased in size, at any rate for some years. The colour of the skin over the nævus was a brownish yellow, and about eighteen months previously some much darker nodules had made their appearance, two or three of which had become almost black. I removed a portion of one of these and some adjacent tissue, and on section it showed some thickening of the horny layer, but much greater thickening of the prickle-cell layer, the papillæ being pressed aside and thinned. Where the non-pigmented passed into the pigmented area, round, oval and fusiform cells made their appearance, some of which contained blackish pigment. Some of these infiltrating cells, however, especially in the upper prickle-cell layer, contained no pigment, and some of the cells contained a lighter brownish granular material. These cells were undoubtedly sarcomatous. The glands in the groin were enlarged.

A well-marked case of Nævus verrucosus such as the above can hardly be mistaken for anything else, and certainly not for a case of Ichthyosis hystrix. A typical case of Ichthyosis hystrix of congenital origin with patches of thickened, hypertrophic warty skin and horny growths resembling rhinoceros skin, forms an entirely characteristic picture, but milder forms of the disease are found in which the spiny growths are not so prominent and which do not

Fig. 1.

Fig. 2.

To illustrate Dr. J. L. Bunch's Article on Ichthyosis hystrix and Nævus verrucosus.

differ very materially from well-marked cases of Ichthyosis simplex. In such cases there are often areas of rough, scaly skin, some of which show warty or spinous projections, either covering large areas of the body, or of smaller dimensions with intervening areas of normal skin. In some instances the spines appear to be cast off from time to time, and subsequently grow again. Mixed cases of Ichthyosis hystrix and Ichthyosis simplex have been recorded by several dermatologists, and such cases cannot but throw some doubt on the fundamental distinction of the two affections. Well-marked cases of Keratosis palmaris and Keratosis plantaris have been described as being cases of Ichthyosis simplex or hystrix, and it is less easy to draw a sharp line of distinction here than between cases of ichthyosis and cases of Keratosis follicularis or Pityriasis rubra pilaris. The congenital origin of the ichthyotic cases serves, of course, as a well-defined means of distinction in many instances, and the histological appearances are often characteristic enough to enable a definite diagnosis to be made. The peripheral neuritis which has rarely been found associated with ichthyosis is not of sufficiently frequent occurrence to form a means of differentiation.

But the cases which most closely resemble one another are cases of linear Ichthyosis hystrix and linear nævus. The distribution is sometimes exactly similar, and clinically the warty, papillary elevations on a rough or scaly surface vary but little from one another in the two diseases, especially when the Nævus verrucosus lesions are free from hair, and only slightly pigmented. Even histologically the characteristics of ichthyosis may not be well defined, and it has been stated by Kaposi that the pathological changes found in ichthyosis hystrix do not differ from those occurring in old warts, while the appearances of a nævus verrucosus section under the microscope would not always permit of an exact diagnosis being made from them alone.

The following is an interesting case of Ichthyosis hystrix of linear distribution. The patient, a woman, aged 29 years, had since birth some well-defined spinous and horny projections, more especially on the extensor surface of one thigh (Fig. 2). This case was under Dr. Radcliffe-Crocker's care for a long time, was diagnosed by him as Ichthyosis hystrix, and eight years previously he removed some of the most prominent lesions. When I saw her the thigh presented

the appearance shown in the plate, the pigmented, indurated, warty masses being arranged in a somewhat linear manner down the anterior surface of the thigh, but whether they followed the line of the cutaneous nerves or blood-vessels it was impossible to say.

Some time before I saw her the lesions had become chafed and inflamed, and some of them were now surrounded by an inflammatory area, and were in places undermined and discharging at the base. The discharge was intensely offensive, and on cultivation showed a growth which consisted chiefly of *Bacillus coli*. I prepared a vaccine with the intention of giving the patient some inoculations, but under simple antiseptic dressings the discharge diminished and lost its offensive characters, and in August of this year I heard that the patient was in New York, and the leg had given no further trouble.

A section through one of the warty-looking masses showed immense hypertrophy of the horny layer. The prickle-cell layer was not increased, the papillæ were not hypertrophied but rather flattened, while the corium was slightly atrophic and infiltrated with large numbers of small round-cells. In the whole of the corium the elastic fibres were atrophic, and in the upper portion apparently absent, Especially in the rete was there a well-marked infiltration of leucocytes. The sebaceous glands were hypertrophied and degenerated.

DESCRIPTION OF PLATE.

FIG. 1.

Nævus verrucosus which has undergone sarcomatous degeneration.

FIG. 2.

Ichthyosis hystrix with linear distribution.

A CASE OF SCLERODACTYLIA WITH SUBCUTANEOUS CALCAREOUS CONCRETIONS.

BY R. E. SCHOLEFIELD, M.A., M.B.,

AND

F. PARKES WEBER, M.A., M.D., F.R.C.P.

A STUDY of the literature of the subject shows the existence of a group of cases characterised by the association of sclerodactylia or more wide-spread sclerodermia with multiple small subcutaneous

calcareous concretions, which in some instances, as in the earliest described case,* have at first been mistaken for gouty tophaceous (uratic) deposits. Chemical examination has, however, shown the concretions to consist of carbonate and phosphate (chiefly carbonate) of calcium, and has likewise demonstrated the absence of sodium urate. The calcareous deposits can of course, as in our own case, likewise be distinguished from uratic nodules by the help of X-rays (skiagrams). The affection is of very slow evolution, and may continue for many years without the patient's general health appearing to suffer. For a long time the fingers or toes may be the only parts affected. The process of calcareous deposition apparently commences about the same time as the sclerodactylia, but probably the calcification is really secondary to the sclerosis, and is largely dependent on degenerative and obliterative changes in the small blood-vessels. Ultimately subcutaneous calcification may occur in other parts of the extremities, and the sclerodermia also may be no longer limited to the hands and feet. In some cases, as in our own case, the onset of the sclerodactylia has been long preceded by vasomotor phenomena, such as the frequent occurrence of local syncope in the fingers (white fingers, "dead fingers") or local asphyxia (cyanosed fingers).

Inflammation frequently occurs around the subcutaneous concretions and gives rise to extreme tenderness. Ulceration often follows, and then the calcareous material is discharged in the form of a chalky fluid, gritty material, or a definite calculus. The ulcers are very indolent, taking a long time to heal. No microbes have been found in the dischage, excepting those due to secondary infection. This process of ulceration, which occurs from time to time at the affected parts, is decidedly painful, so that there is no resemblance to the "painless whitlows" of so-called "Morvan's disease," and the finger-changes met with in the so-called "Morvan type" of syringomyelia. The fingers or toes become thickened, stiffened, deformed and shiny. Sensation is blunted over the diseased portions, and the normally soft pulpy cushions of the tips of the fingers or toes may gradually become almost as hard as stone. The metabolism has, as far as we know, not yet been specially investigated in order to throw light on the tendency towards calcareous deposition.

* Described by a Swiss doctor, H. Weber, see *Correspondenzblatt für Schweizer Ærzte, Basel*, 1878, vol. viii, p. 623.

These cases are sharply distinguished from all the following kinds of subcutaneous or cutaneous calcification:

(1) Calcification in sebaceous cysts, sebaceous adenomata, and so-called "benign epitheliomata" (A. Malherbe, W. von Noorden, etc.), and in cystic adenomata connected with the sweat apparatus (H. D. Rolleston).

(2) Calcification in lipomata, fibromata, carcinomata, and other tumours.

(3) Calcification in tuberculous caseous nodules or in other subcutaneous chronic inflammatory nodules or scars.

(4) Calcified subcutaneous cysticerci.

(5) Calcification in subcutaneous veins (subcutaneous phleboliths) and subcutaneous arteries.

(6) Calcareous metastases in the skin (J. Jadassohn).

(7) Calcification of minute subcutaneous fat-lobules ("Fettgewebssteine") in front of the tibiæ of elderly persons.*

(8) True bone-formation in subcutaneous tissue or in scars.

We shall make no attempt here to analyse the literature on the class of case now under consideration. This has been quite recently dealt with by G. Thibierge and R. J. Weissenbach in their admirable monograph on the subject.† No similar cases have, as far as we know, been described in English or American literature. Yet it is quite possible that certain cases classed as examples of chronic Raynaud's disease with hypertrophic sclerotic reaction of the soft parts, and terminating in a condition of sclerodactylia with shortened, thickened, hard, deformed, scarred fingers, may really have been examples of the same affection, and the extruded calcareous material may have been mistaken for fragments of necrosed bone.

The patient (E. M. D—) in the present case is an unmarried woman,

* O. M. Chiari ("Ueber die herdweise Verkalkung und Verknocherung des subcutanen Fettgewebes," *Zeitschrift für Heilkunde*, 1907, vol. xxviii, Supplementheft, p. 1) agrees with E. H. Bennett ("On Calcification of Adipose Tissue," *Dublin Journ. Med. Sci.*, 1878, vol. lxv, p. 19), that the small, freely movable calcareous nodules not rarely met with in front of the tibiæ in elderly persons, especially women, are due to calcification of fat-lobules, and not to calcification in veins, arteries or lymphatics. Chiari thinks that the cause of this calcification is interference with the local blood-supply caused by chronic deforming endarteritis.

† G. Thibierge and R. J. Weissenbach, "Concrétions calcaires sous-cutanées et sclérodermie," *Annales de Derm. et de Syph.*, Paris, 1911, vol. ii, pp. 129–155.

aged 50 years, of medium height, rather thin, active in her habits, and mentally normal. She looks rather younger than her age, and the menopause has not yet arrived. As a child she used to be subject to red hands and to chilblains in her hands and feet, that is to say, she might be said to have had a so-called "bad circulation in her extremities." When about twenty years of age she began to be often troubled by her fingers "going dead"; they used to become white ("local syncope"), not purple or black ("local asphyxia").

This occurred especially in cold weather, and she formerly often bathed them in hot water to take away the numbness. After exposure to cold the sensation of "pins and needles" was sometimes very disagreeable when her fingers were "coming to" again. Since the age of thirty-five years the skin and soft parts of her fingers have been gradually becoming harder and stiffer so as to constitute a condition of sclerodactylia. From time to time indolent, painful ulceration has occurred on the fingers, chiefly at the tips, giving rise to a gritty discharge. In April, 1911, Dr. Scholefield removed a little subcutaneous concretion from the back of the middle segment of the fourth finger of the right hand, and found it rather a difficult task because it was firmly embedded in a dense meshwork of fibrous tissue. About three years ago an area of swelling and redness appeared over the left olecranon. This ulcerated and was scraped out by Dr. Scholefield, who chemically examined the gritty material which he removed, but with negative result in regard to the presence of urates. Excepting for these troubles and appendicitis (for which the appendix was successfully removed ten years ago), she has on the whole enjoyed good health. She has never been out of England except for visits to the Continent. There is no history of any similar disorder in the family. Her father died at sixty-four years (of cholelithiasis?), and her mother died recently of pneumonia at over eighty years of age.

Present condition.—The ends of the fingers have the characteristic appearance of sclerodactylia, and in addition to that there are scars from which gritty material has been extruded. The terminal segments of some of the fingers appear shortened. The flesh over the flexor aspects of the terminal phalanges of the second, fourth and fifth fingers of the left hand seems particularly altered and feels quite hard as if subcutaneous calcification had taken place. Indeed,

the tip of the little finger is white and looks as if some calcareous material was shortly going to be extruded. Owing to the thickening and hardening of the soft parts, movement in some of the finger-joints has become diminished. There is no true dissociation of sensation anywhere, but all sensation is somewhat blunted over the portions of the fingers where the skin has become callous.

The presence of calcification in the fingers is confirmed by examination with Roentgen rays, as it also has been by means of incision. Skiagrams of the left hand (see illustration) reveal considerable calcification in front of the terminal phalanges of the second, fourth and fifth fingers, and likewise a little at the tip of the thumb. In skiagrams of the right hand (see illustration) one can make out a little subcutaneous calcification in several fingers (this is, unfortunately, not all shown in the skiagram selected for illustration), less than in the left hand, but not so confined to the terminal segments. The distal portion of the terminal phalanx of the right middle finger has disappeared.

The patient's feet show nothing abnormal either by ordinary examination or by skiagraphy. There is apparently no sclerodermatous change anywhere except in the hands (sclerodactylia). The pinnæ of the ears show no concretions of any kind. There is no thickening of the ulnar nerves. There is slight redness and swelling over the right olecranon. This has only recently been observed, and resembles the redness and swelling over the left olecranon, which, as has been already stated, occurred three years ago, and resulted in a discharge of gritty material. Skiagrams of both elbows show nothing abnormal except a minute calcareous speck over each olecranon. The knee-jerks are natural. There is no evidence of any disease of the thoracic or abdominal viscera. The urine is free from albumen and sugar. No examination of the patient's metabolism has yet been made. There is no evidence of any congenital or acquired syphilitic taint.

That the subcutaneous concretions in this case are not of the nature of gouty (tophaceous) deposits is abundantly proved by their opacity to Röntgen rays, and by the fact that Dr. Scholefield examined the gritty discharge from the left olecranon with negative result in regard to the presence of urates.

The appearance of the fingers to some extent reminds one of the

FIG. 1.—Skiagram of left hand, showing subcutaneous calcareous concretions in front of terminal phalanges.

FIG. 2.—Skiagram of right hand. Note calcareous deposit at the tip of the index finger.

TO ILLUSTRATE THE ARTICLE ON SCLERODACTYLIA WITH SUBCUTANEOUS CALCAREOUS CONCRETIONS BY DR. R. E. SCHOLEFIELD AND DR. F. PARKES WEBER.

stumpy thickened fingers in the so-called "Morvan type" of syringomyelia, but there is no "dissociation of sensation," and the ulceration (giving rise to the gritty discharge) has been associated with great local tenderness and has been therefore quite different to so-called "painless whitlows."

In conclusion we have to thank Dr. G. Dorner for the excellent skiagrams which he kindly made for us.

DISCOLORATIO UNGUIUM: (1) LEUCOPATHIA UNGUIUM; (2) UNGUES FLAVI.

By W. KNOWSLEY SIBLEY, M.A., M.D., B.C., M.R.C.P.

(1) Leucopathia unguium.

The following is an interesting example of the above disease, which occurred in a man who presented himself at the St. John's Hospital for Diseases of the Skin, London, suffering from scabies. A healthy man, aged 25 years, a hairdresser by occupation, who stated that for some fifteen years he had noticed transverse white bands appearing and disappearing on each of his finger-nails. The bands generally commenced at the base of the finger-nail, and gradually with the growth of the nail moved towards the free end. He stated that occasionally a band would appear or disappear more or less suddenly on any part of the nails. For instance he would wake up in the morning and find a new band which was not present on the previous night. These acutely arising bands generally appeared towards the free end of the nails.

At the time he came under my observation, with the exception of the nails of the left little finger, and the ulnar half of the ring finger of this hand, all the finger, and both the thumb-nails were affected; each nail had one, two or three, more or less complete even bands right across the nail, as is well shown in the accompanying photograph. The area of the left ulnar nerve distribution was unaffected, there being a marked band on the radial half of the nail of the left ring finger, but none on the ulnar half of this nail, nor on that of the little finger. I observed that a distinct band which was

present and showed very clearly in the photograph which was taken on December 12th, on the nail of the right little finger, had quite disappeared by the middle of the following January ; the other bands had remained much the same, and no fresh ones had appeared.

The nails of the toes were affected to a lesser degree; they were mostly thickened, ribbed, and had a tendency to grow over at the extremity. Bands were present on some of the nails, but they were much less distinct than those on the fingers.

As regards other epiblastic tissues, the teeth were small, ill-developed, discoloured and carious. The hairs from the dorsum of the fingers were a little atrophied. Those from the head were more or less normal in character.

Microscopical examination of sections of these nails, which had been decalcified by nitric acid and stained with safronin, showed that the band regions took the stain very readily, and appeared to be a mass of partly cornified layers of cells in several strata, with spaces between. Large cells which had retained their nuclei were clearly definable.

This condition appears to reveal the fact that the cells and tissues in the regions of the white bands took the stain more readily and showed the structure of the nail-cells, which had mostly retained their nuclei, and therefore had not undergone keratinisation like the cells of the normal nail-structure.

There were several spaces between the laminæ of the matrix substance which might be mistaken for air-spaces, but were, I believe, produced by the razor when cutting through structures of unequal density.

The disease might therefore be described as a trophoneurosis, leading to nutritional changes in the nail-substance.

I should therefore describe the condition of bands to be due to a failure of the natural process of cornification. The histology of these bands is more or less that of the normal lunula of the nail, the cells of which, being more or less opaque, prevent the vascular bed of the nail-matrix being shown through the nail-substance, hence its whitish appearance in contrast to the pink colour of the rest of the nail.

If this explanation of the pathological condition is the correct one, it is easy to understand how these bands may rapidly disappear, by a process of natural cornification of their cells, as in the case I have

described. It is, however, quite a different matter to explain the more or less sudden appearance of bands towards the free margin of the nails, but I consider the patient's statement as to this phenomenon requires confirmation, as I did not observe this to happen while he was under my observation. It is quite probable that a band close to the base of the nail might remain for some time unnoticed, and that only when it approached the middle or top of the nail that the atten-

tion of the patient would be drawn to it, and his conclusions, therefore, as to its origin, quite false.

This curious and somewhat unusual pathological condition of the nails is also known by the following names: Achromia unguium, Leuconychia, Albugo, Flores unguium, white spots, white nails, gift or fortune spots, lies, etc., and to the French as *décoloration des ongles*.

The varieties of this condition are generally grouped under the heading of Atrophia unguium, but I consider they should form a distinct class, as there does not appear to be any atrophy or malformation of the nail; in fact, in most of the cases which have been

described, especially those accompanied by photographs or drawings of the condition, the nails themselves are well developed, and well preserved, and it is only in the remarkable coloration that anything abnormal shows itself.

I would describe two subdivisions of the condition:

(1) The congenital and permanent, which may be associated with changes in the hair, and possibly of the teeth.

(2) The acquired and more or less temporary, in which the hair and teeth do not reveal anything abnormal.

The case I have described was probably an example of the congenital type.

The following are the cases of this condition previously published:

Langdon Down (1) described the case of a professional man who had two distinct sets of white lines extending transversely right across his fingers and toes, especially marked on those of the left side, which followed two attacks of nervous breakdown. These illnesses were accompanied by corneal ulceration, intermittent heart's action, and great general nervous prostration, the result of over-work. The

lines in the nails corresponded with the times of the occurrence of the two distinct attacks of illness.

Morris Longstreth (2) wrote a paper entitled "Changes in the Nails in Fever," in which he described some white bands which appeared in his own nails, after an attack of relapsing fever, and which bands occurred at the time of each relapse.

De Costa (3) at the same meeting showed a case of a boy, aged 13 years, who had recently recovered from a prolonged attack of typhoid fever with relapses, and who developed white bands on his nails, which he then described as "anæmic streaks." Associated with the bands were alterations on the surface of the nails, which were slightly ridged, and so the transverse bands could be felt as well as seen. Similar, but less distinct marks, were present on the toe-nails.

Morrisson, of Baltimore (4), published the case of a man, aged 20 years, who suddenly developed bands on his finger-nails, and these disappeared after a few months. The plate shows that the bands were not completely across the nails, but only in irregular wavy lines. The toe-nails were not affected.

Bielschowsky (5) reported the case of a man suffering from multiple neuritis, in whom white spots appeared on the lower part of the finger-nails, which spots rapidly grew and coalesced into bands extending across each nail. The bands were milky-white in the centre, and became paler and more pink towards the ends. The nails of the toes were not affected.

Unna's case (6), described as one of leuconychia and leucotrichia, was probably congenital, and the hair of the head presented a partial appearance of the condition known as ringed-hair. It occurred in a man, aged 26 years, a joiner by trade, who stated he noticed the changes in his nails when he was a child. After an injury, when he was eleven years old, the nails of the two injured middle fingers became red, but afterwards they assumed their natural colour. He never had any inflammatory mischief of the nails, and he believed them to have been congenital. The toe-nails were not affected.

Herman Lawrence (7) records a case of an apparently healthy middle-aged man which was probably congenital. The nails on the fingers of this patient's son, who was five years of age, presented a similar appearance, but not so marked a degree as those of the father.

Stout (8) described the case of a man, aged 21 years, a waiter, who had some scrofulous glands, and was in a somewhat nervous condition. He had wavy white lines and spots on the nails of the fingers, and to a lesser degree on the toe-nails. The bands were constant and probably congenital.

W. Sykes (9) stated that in his own person he could produce white specks on his finger-nails by scraping, pressing back, and cutting the fold of the nail over the lunula.

Heidingsfeld (10) collected seven cases, six of which were in young women, from sixteen to thirty years of age, all of whom manicured their nails assiduously, and the bands or striæ were most marked on the nails of the right hand, that is, on those the more liable to injury by unskilled manipulation by the left hand. He considered that all of his cases were the result of injury to the nail-fold by manicuring operations.

Unna makes three divisions of this condition, which he designates as follows:

(1) Leuconychia punctata: white spots.

(2) Leuconychia striata: white bands or striæ.

(3) Leuconychia totalis, which condition involves the nail in its entirety.

Although in some of the cases recorded the temporary occurrence of white bands is clearly demonstrated to be the result of a general constitutional disturbance, such as typhoid fever, relapsing fever, nervous breakdown, etc., the pathological result is quite different from that much more common condition of transverse furrows or ridges on the nails corresponding to a period of illness of an acute character, such as after many fevers, measles, typhoid, pneumonia, etc., during which attack there is a consequent malnutrition and arrest of growth of the nails, stated to be most marked on the thumbs, and next on the index fingers.

Changes in the nails accompanying general illness were first described by Reil, of Halle (11), in 1792, and again more fully in his work *On the Diagnosis and Treatment of Fevers* (12), published in 1804. Beau (13) in 1846 also drew attention to the subject, and calculated that the nails of the fingers grow at about the rate of a millimetre a week, which for an average nail would mean five months, for a whole nail, or rather more than two nails a year. The nails of

the toes grow more slowly; that of the great toe takes four times this period. It becomes, therefore, a matter of easy calculation to fix the date of an acute illness or illnesses by the relative position of furrows on the nails.

Samuel Wilks (14), in the *Lancet* of 1869 and 1870, recorded several cases of furrows on the nails as the result of acute illness, such as in a case of severe diarrhœa accompanied by great prostration, scarlet fever, a sharp attack of gout, acute rheumatism, diphtheria, and one after starvation. His most remarkable case (15) was that of a healthy, well-developed, robust man, who, on August 29th, and again on October 18th of the same year, suffered for three days from severe sea-sickness, after which all the nails on both his hands showed two distinct furrows, the position of which corresponded to the dates of the two attacks of sea-sickness.

Murchison, (16), in the second edition of his work on *Fevers*, also drew attention to the subject.

Hutchinson (17) described furrows on the nails, especially after febrile and gouty attacks of illness, and records a case where bands of hæmorrhage appeared in the nails after one illness and furrows after another. He considered that white spots were often due to picking back the nail-fold, and might co-exist with similar white spots on the teeth. In relapses, for instance, in cases of typhoid fever, a second furrow might appear on the nails as a record of the fact. An analogous condition occurs on the hoofs of animals after severe illness, and the horns of cows often show a similar change after each parturition. The same markings have been observed on the wing- and tail-feathers of domestic fowls and other birds in captivity. Unna and Joseph (6, 19, 20, 21) consider that in microscopic examination of these cases the nails reveal the presence of air-spaces in the nail-substance, and hence the white colour similar to those which have been described as being present in white hairs. According to Giovannici (18) the condition is due to abnormal cornification. Heidingsfeld (10) states that the white bands consist of cells which retain their nuclei, stain freely, and preserve their original form, due to failure to undergo physiological keratinisation and not to infiltration of air. He says that leuconychia is the result of some pathological change of the structure in the plane of the nail-cells, approximating a failure of the affected cells to undergo normal physiological keratinisation. The causes may

be traumatic, malnutrition, febrile disease, neuroses, or any agency which disturbs the growth, development or keratinisation of the matrix-cells in their change into nail-substance.

(2) Ungues flavi.

The following is a case of Ungues flavi, that is, nails of a yellow-ochre colour, which has recently been under my observation. The patient was a fairly healthy, somewhat nervous type of young man of frail build, aged 23 years, who two years previously, in October, 1908. had contracted syphilis. He had had a chancre followed by an ulcerated fauces and a general adenitis, but no secondary rash.

He had been strictly under mercurial treatment by grey powder in pill form from the earliest sign of the disease. In September, 1909, these were replaced by hypodermic injections of succinimide of mercury, somewhat irregularly, about twice a week. He had never been salivated or shown any evidence of mercurialism. At the time the nails underwent the change, I am about to describe, there were neither signs nor symptoms of the previous disease about him, and in October, 1910, the Wasserman reaction was negative.

During the month of June, 1910, the nails of the fingers and of the thumbs on both hands were becoming discoloured and assuming a uniform yellowish tint. The change was slow, but after a few months the nails were all of a deep yellow-ochre colour and noticeably thickened throughout, but they remained quite smooth and even on the surface. The toe-nails also showed evidence of the same pathological changes, but to a lesser degree. In most of the finger-nails the lunula had completely disappeared by January, 1911, and all the nails were still thicker and of a deeper yellow-ochre colour.

They had the appearance of being stained by nicotine, as is often seen in inveterate cigarette smokers, but this patient smoked but very little, and all the nails on both hands were equally affected, and there was no staining of the neighbouring skin of the fingers. There was no jaundice at any time present.

During the whole of this period there was almost complete arrest in the normal growth of the nail in length, but all the time they were growing in thickness, in fact it might appear that the natural growth in length was replaced by an unnatural increase in thickness.

In March of this year a specimen of the left index nail was taken for microscopical examination.

He ceased the mercurial treatment at the end of 1910, and commenced taking small doses of iodide of potassium in January, 1911, first in the form of the pure salt, which he did not take well, and so it was replaced by ioglidine tablets, which he took without any unpleasant symptoms. I prescribed a salicylic acid ointment to be applied to the nails.

By the end of March there was a marked improvement in the condition of his nails. The natural colour was gradually returning, and the lunulæ, which had completely disappeared from all the nails, was reappearing on some of them. The improvement, or return to the normal condition, first showed itself at the proximal or base of the nails with the reappearance of the lunula, and at the time I examined the case at this stage, there was a marked line of demarcation between the normal and the pathological condition across some of the lunulæ, especially marked on the nail of the right index finger, showing that the return to the normal growth had been more or less sudden in its appearance.

When seen again, about the middle of July, the nails were practically normal, and a few weeks later quite so, both as to the coloration and thickness.

There was no obvious change noticed in the hair, except that it was coming out a good deal, and he was getting rather thin on the vertex.

Microscopical sections through the free end of the nail, which had been decalcified with nitric acid, and afterwards stained by Gram's method, showed there was considerable increase in thickness of the whole nail, and the centre and deeper layers of the nail-matrix took the stain but very slightly. The superficial layers of the nail-substance took the stain fairly well, and revealed the presence of large, well-defined, nucleated nail-cells. The cells of the deeper layers were much less defined, but there was no evidence of any gross structural change in the planes of the nail-substance.

The questions that naturally arose as to the ætiology of this condition are, was it an unusual feature of syphilis, or due to the mercury? The general state of the patient's health at the time was not quite satisfactory, but there was no obvious lesion for diagnostic purposes.

So, again, was the return to the normal due to taking of the iodide, as he was taking iodide of potassium and ioglidine tablets all through the period of the improvement ?

In the *International Atlas*, of 1891, von S. Giovannici (18) pictures and describes a case of white nails under the title of "Canities unguium," which he saw in a coachman, aged 29 years, and of a robust constitution. The whole of the nails were white, in fact nearly an ivory-white colour and well preserved. The condition came on at the age of twelve years after a moderately severe attack of typhoid fever. Histologically he detected the presence of air in the nail-matrix, and he considered the condition analogous to the deterioration of the nails which is characterised by white opaque spots in the shape of dots, or of transverse stripes. The nails of the toes were not affected.

Judging by the plate published of this case, the whole nail appears to have assumed the colour, texture, and condition of the lunula of the nail in its normal condition, but possibly the whole matrix was thickened.

It is known that the nails of convalescents from malignant fevers may become white for a time, and that the nails of a chalky hue have been described in paralytics.

Max Joseph (19) recorded a case of white nails occurring in a healthy man, aged 20 years, a butcher, whose finger-tips became swollen and painful; after this subsided the nails turned partly white, and later on he published a second case (20) in a young girl suffering from anæmia, and later published an interesting article upon "Diseases of the Nails" (21).

Parkes Weber and Creig (22) described the case of a man, aged 52 years, who had also rheumatic valvular disease of the heart. He had noticed that his nails had become white for some four years. All the finger-nails were white, and no lunula were visible; they were rather flat, and one was almost in the condition known as spoon-nail; they were also somewhat thinner than normal, and presented longitudinal grooves. The condition was less marked on the toe-nails. The patient also had some chronic rheumatoid deformity of the small joints of his hands and feet.

Professor E. Geber (23) published in 1885 an article entitled, "Discoloratio unguium: Morbid Changes of the Nail and its Bed," in

which he said that in cases of cyanosis and during attacks of intermittent fever the nails became livid. In convalescence from feverish attacks white, in anasarca light white, in icterus yellow, in consequence of apoplexy dark brown, in hectic conditions pale, and with certain diseases of internal organs grey.

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NOTE ON THE ÆTIOLOGY OF LEPROSY.

By WILLIAM TURNER, M.A., M.D., Gibraltar.

Notwithstanding that repeated attempts have been made at the instance of the Colonial Office, the Royal College of Physicians, and other interested bodies, to solve the question of the ætiology of leprosy, by sending to various parts of the world commissions equipped with this object in view, and in spite of the fact that these expert commissioners have almost unanimously reported their conviction that this disease is not propagated by contagion except in very

rare instances, the subject of the causation of leprosy remains still shrouded in a veil of mystery. Large sums are still being devoted, in certain of our colonies, to the maintenance of leper establishments, an expenditure which ought to be largely curtailed were the findings of these investigators believed in and acted upon. A most important advance in the inquiry was undoubtedly made by the discovery of the essential microbe—the *Bacillus lepræ*—by Hensen of Bergen in 1874, but the complete life-history of this bacillus and its channels of entrance into the human system have yet to be determined. There does not at present exist any general consensus of medical opinion on this subject.

The case to be related is in some respects a unique one, and may help to limit the inquiry which aims at the elucidation of the ætiology of this dread disease.

The patient was an imbecile, who was admitted at the age of twenty-eight to the Gibraltar Lunatic Asylum in the month of June, 1883.

Family history.—His father, an Italian by birth, was a carpenter in the Gibraltar Port Department, and lived for many years in a stationary ship in the harbour. He was a very healthy man, and died of old age at 94. His mother, a native of Gibraltar, died at the age of 87 from a like cause. Two sisters are alive, both of highly neurotic temperament, but quite healthy. Of two brothers, one is now in the lunatic asylum suffering from dementia with epileptic tendency; the other, a confirmed drunkard, is a carpenter by trade. A cousin is an inmate of the lunatic asylum, a chronic imbecile. There have been other evidences of insanity in the family, all traceable to the mother's side. None of these relatives have presented any signs of leprosy.

Patient's history.—He is said to have been imbecile from his birth. He never had any education, and never followed any employment nor earned his own living, but passed his time in wine-houses as a buffoon for the diversion of customers, who supplied him with drink. At the age of twenty-eight he was admitted to the lunatic asylum at the request of his family.

From the time of his admission till the year 1902 (*i.e.* for nineteen years) nothing remarkable in the patient's condition took place. He showed no signs of physical defect or disease of any kind.

He employed himself mainly in gardening and scrubbing floors, cleaning utensils, etc. In 1902 his hands and feet became affected with dusky red thickenings on their dorsal aspect, and pinkish swellings appeared also on the face, especially on the brow and eyebrows. It was not until May, 1903, that this affection of the skin suggested the idea of leprosy. (He had, indeed, been treated for some time with mercury on the suspicion of its being syphilitic.) From that time the leonine configuration of the face began to assert itself. The case was then isolated, and measures taken for keeping separate his clothing, feeding utensils, washing arrangements, etc.

As years passed the patient remained in good general health. The hands gradually became more deformed and the face more disfigured. Sometimes the affected parts would appear more deeply congested and swollen than at other times, but the hard callous folds on the forehead and eyebrows never diminished in size, and dark pigmentation of the skin supervened.

In March, 1906, one of the toes became erysipelatous and eventually dropped off. The extensor aspect of the forearms, the shoulders, and the chest became studded with brown tuberculated swellings, and ulcers formed on the elbows. Opacity of the corneæ set in, and the voice became aphonic from swellings in the mouth and pharynx. Finally all forms of nourishment were rejected, and the patient died exhausted on September 21st, 1906.

Thus the case from beginning to end was typical of the tuberculated form of leprosy. The presence of the *Bacillus lepræ* was abundantly demonstrated in specimens taken from the hypertrophied tissues of the forehead.

Now the question which presents itself is: How came this man to be affected with leprosy?

No case of leprosy has occurred amongst the inhabitants of Gibraltar for a great many years, certainly not within the past thirty years to my own knowledge. There is no record that the disease has ever been endemic here. The patient in question, born and reared in Gibraltar, had been an inmate of the lunatic asylum for nineteen years before he became affected with leprosy. He had had no communication with the outer world during that time, except by the visits of his sisters for half an hour once a fortnight, and the sisters showed no signs of the disease. It should be stated also that

Gibraltar may be regarded, to all intents and purposes, as an island. The town is entered from the mainland by only one narrow road, and the lunatic asylum occupies an isolated site half a mile beyond the town. Its gardens are fenced in by high retaining walls outside of which the patients do not pass. The idea, therefore, of a *contagious* origin in this case seems absolutely untenable.

The question likewise of an *hereditary* origin appears to be answerable only in the negative, seeing that neither parents nor any known relative ever manifested any evidence of the disease.

Insanitary conditions of life, *uncleanliness*, of person or of abode or of clothing may similarly be eliminated as impossible causes in this case, for the accommodation in the asylum is ample, well ventilated, almost luxurious, and the washing and bathing arrangements receive the utmost attention.

Emanations from the soil have been suggested by some authorities as possible carriers of the virus of leprosy, but in this case there is no history that the disease has ever been endemic here so as to contaminate the soil, at all events not for centuries past, and one can hardly conceive of the bacillus remaining effective in the soil after so long a period, even if it had existed centuries ago.

The problem of causation, therefore, so far as affecting the present case, appears to resolve itself into a question of *food supply*, all other considerations having failed to help us in our inquiry. The dietary provided in the asylum is a liberal one and includes a large proportion of fresh vegetables and also fresh meat. Up to the year 1900 a ration of salt pork was issued once a week, but this was then struck off as it was suspected of having been the cause of an outbreak of dysentery. Up to the year 1903 two rations of fish were issued weekly, one of fresh fish, the other of dried salt cod fish. The latter was then omitted from the dietary on the appearance of the case of leprosy.

Whether or not the salt pork or the dried salt fish can be held in any way answerable for the case in question, or are to be regarded in the light of simple concomitants, were hard to say, but the coincidence is interesting in view of the theory held by Sir J. Hutchinson that dried and decomposing fish is to be regarded as the true cause of leprosy.

CLINICAL NOTE.

BULLOUS ERUPTION ASSOCIATED WITH APPENDIX ABSCESS IN A CHILD OF THREE.

By J. H. SEQUEIRA, M.D., F.R.C.P.

On May 2nd last, Dr. Phillips, of Beckenham, asked me to see a little boy, aged 3 years and 4 months, suffering from a bullous eruption. I had previously seen the child's father and sister on account of psoriasis. The child had had excellent health until March, 1911, when blebs appeared on the upper and lower extremities. The attack lasted for a little over a week, and then the blebs dried up, leaving no scar. A second attack of similar character followed after a short interval, and the third attack, that for which I was consulted, had been present one week.

The patient when stripped was a finely developed child, apparently in the best of health, and full of spirits. There was a copious eruption of blebs of a hemispherical shape grouped in the extremities, the distal parts being chiefly affected. There were more bullæ on the extensor than on the flexor aspect. The blebs formed on healthy skin, and their contents were quite clear, yellowish serum. There was no erythema present. The eruption itched very much, but the pruritus was not confined to the affected areas.

There was no opportunity to examine the contents of the blebs or of the blood, but the eruption and its tendency to recurrence suggested the beginning of Dermatitis herpetiformis.

The same night the child was taken suddenly ill with severe abdominal pain, but the pulse and temperature were normal. The next morning the pain was very severe, the lower abdomen rigid, and a mass was felt in the right iliac fossa. Temperature 101° F.; pulse 140; respirations 40.

The child was removed to Charing Cross Hospital, and Mr. Stanley Boyd operated and found two to three drachms of pus in a gangrenous, perforated appendix, the omentum being matted by adhesive lymph. The cavity was drained. The temperature became normal in four days and remained so, the child making a perfect recovery. The

bullous eruption disappeared in a week without any treatment, and has not returned.

I am indebted to Mr. Stanley Boyd and to Dr. Phillips for their notes of the case, which I think worthy of record as throwing some light upon the difficult question of the causation of these anomalous bullous eruptions. I regret that there were no opportunities for a full examination of the blood and the contents of the bullæ, but in view of the probable long duration of the purulent collection in the appendix it appears unlikely that there would have been an excess of eosinophiles.

CORRECTION.

In Dr. Dyson's article on "Cutaneous Pigmentation," on page 208, *for* "ferrocyanide," *read* "ferricyanide," the formula reading as follows:

Borax	40 grms.
Ferricyanide of potassium . .	50 ,,
Water	2000 c.c.

CURRENT LITERATURE.

SPOROTRICHOSIS IN MAN, WITH INCIDENTAL CONSIDERATION OF ITS RELATION TO MYCOTIC LYMPHANGITIS IN HORSES. James Nevins Hyde and D. J. Davis. (*Journ. of Cut. Dis.*, July, 1910.)

On December 3rd, 1909, a farmer, aged 24 years, from North Dakota, was brought to Prof. Hyde with a disease which had been diagnosed as possibly farcy. The history obtained was that about forty to sixty days previously a pustule formed on the back of the left hand, and gradually enlarged and became much inflamed, spreading somewhat rapidly over the forearm to the shoulder. Then some papulo-nodules evolved, some as big as a horse-chestnut, and all contained pus. There had been some slight febrile disturbance. The man had been treated with a bichloride of mercury dressing locally, and by the ingestion of potassium iodide. This treatment was continued, and the patient eventually recovered.

The *Sporotrichium Schenckii* was cultivated from the lesions, and successfully inoculated into white mice, white rats, and a monkey (*Macacus rhesus*). Smears

of pus and sections of diseased skin did not display the fungus, but was easily detected in the infected animals.

Now in the year 1909 an epidemic affecting horses had occurred on a farm in North Dakota, next to that occupied by the farmer consulting Hyde. The epidemic was diagnosed as one of glanders, but the bacilli were not isolated and the mallein test was not applied. The horses suffered from a profuse and exceedingly fœtid nasal discharge, deep ulceration of the septum nasi, and dense induration and enlargement of the lymphatics. From the same district in 1904 Dr. Quain published a report of six patients infected with a peculiar disorder, and in May, 1910, six further cases had been seen. In these cases the infection occurred through an invasion-atrium, followed by lymphatic complications, the involvement of the axillary and other glands in about three months. The disease was cured by radical excision and cauterisation and by X-rays.

The probability that the disease in the horses and men was of similar nature is evident, and the proof of sporotrichosis in Hyde's patient might give the clue to the nature of the whole epidemic.

Further, the authors studied an organism isolated from mycotic lymphangitis in the horse infected in Pennsylvania, obtained from Dr. Mohler, and this organism was found to be similar to that obtained from the man described in morphology, cultural characteristics, and effects of inoculation in rats and mice.

The literature setting forth the characters of human sporotrichosis is then reviewed, and the relation of *Sporotrichium Schenckii* to the organisms found in the horse disease, which is known under many titles by veterinarians as distinct from glanders. In this horse and mule disease there occurs, in most cases after an invasion-atrium produced by trauma and an incubative period of three to twelve weeks, lachrymation, corded lymphatic vessels, enlarged glands, and numerous isolated, tumour-like swellings, hard or soft, furnishing a sero-sanguinolent pus, and often breaking down into ulcers. In many cases there has been perforation of the septum nasi. One extremity may be chiefly involved, and then often with elephantiasis. The systemic symptoms are often slight. The diseased animals do not respond to the mallein test, and the autopsies show chiefly lung abscesses. These cases are singularly alike, and strikingly resemble sporotrichosis in man, but few cases are on record of the transmission of the disease from the horse to man.

The problem arises whether the horse epidemic in Dakota was not really "mycotic lymphangitis," and this disease was definitely reported in that place in 1908. The authors point out the discovery of various organisms in the horse disease, especially a so-called *Saccharomyces farcinosus*, by Tokiskige in Japan, which is widely different botanically from sporotrichium. Possibly this mycotic lymphangitis of horses is caused by more than one organism. This interesting paper is well illustrated by plates, and terminates by a copious bibliography.

T. C. F.

LICHEN NITIDUS. Richard and Sutton. (*Journ. of Cut. Dis.*, November, 1910.)

The author reviews the literature on this subject, and records a case of his own. Pinkus in 1901, and later, recorded eighteen cases and described the

eruption as a papular eruption of the skin, characterised by the presence of numerous sharply defined, flat-topped, shiny, pin-head-sized papules without any tendency to grouping or confluence, and practically of the same hue as the surrounding skin, and without subjective symptoms. The eruption favoured the genital region, but might occur on the abdomen, breast, and arms. Obviously the eruption may suggest Lichen planus, but is said to differ by the absence of itching, in the colour, distribution, absence of increase in size, and absence of coalescence. It is distinguishable also from plane warts. The papules are described as formed of granulomatous tissue in the upper cutis, closely adjacent to the epidermis, which also is characteristically altered and much cornified. Arndt, in Lassar's clinique, described thirteen cases, all males, and from twelve to forty-five years of age. He thought the histology that of an infective granuloma, probably an atypical tuberculosis. In Sutton's case there was an oval patch of flat-topped, shiny papules on each anterior axillary fold, also in groins, around the umbilicus, and on the upper anterior surface of each forearm, the flexor surfaces of the wrists, and extensor aspects of thumbs. From histological examination Sutton concluded the lesion was a granuloma, but not tuberculous.

T. C. F.

A CASE OF VERRUGA PERUVIANA WITH SUCCESSFUL INOCULATION OF AN APE. Jadassohn and G. Seiffert. (*Zeitschr. für Hygiene und Infektionskrankheiten*, 1910, Bd. lxvi, p. 247.)

The patient was a Swiss, who was acting as a guide in Peru. Except for suffering for a time from the intense cold the patient remained otherwise healthy, but noticed a week after he had returned home certain peculiar sensations on being in a heated room. He had a general feeling of malaise followed by profuse perspiration. A few days later he noticed a small papule on his left leg, which was soon followed by a second on his left cheek, and within fourteen days he had several on his face and arms. During this time there were no subjective symptoms. In this condition the patient was admitted into hospital, where nothing else abnormal was found. The papules were about the size of a small cherry, having a dark violet-red colour and raised above the surface of the skin with no surrounding inflammation. The surface was smooth and stretched, the consistence soft and elastic, and quite painless. There was a lesion in the left eye on the conjunctiva bulbi. Wassermann negative; Pirquet's reaction strongly positive. Injection tuberculin: no reaction, and only a rise of temperature to 38° C. after 1 mgrm. No local reaction. Diagnosis first made was multiple angioma or hæmorrhagic sarcoma. Histologically the lesion was a granuloma. All attempts at finding a specific organism proved fruitless. According to Odriozola the disease occurs spontaneously in several animals, the lesions often being very large, and in animals also fever precedes the skin-eruption. A bitch was inoculated with the blood from one of the tumours, and after some similar lesions had appeared, which ulcerated and bled, the dog died. Other animals, except an ape, were unaffected. The incubation period was forty-five days, in the second generation fourteen days, and in the third generation only a week, probably dependent upon the increase of virulence. The disease in apes healed spontaneously and the ape was immune to further infection.

J. McD.

THE INFLUENCE OF MERCURY UPON THE WASSERMANN'S REACTION. Karl Marcus. (*Archiv f. Derm. u. Syph.*, Bd. cvii, Heft 1–3, p. 17.)

Only Wassermann's original reaction was employed. It was found that the longer the syphilitic virus had been in the body and the greater the frequency of recurrences, so much stronger was the anti-body content of the serum, and so much more difficult was it to influence it by treatment. The sooner mercury was given after infection, greater was the influence treatment had on the anti-body content. The more courses of treatment the patient had undergone, the more likelihood was there of obtaining a negative reaction. The influence of the early courses of bringing about this change was more marked than the later.

The author had thirteen cases in which the treatment was begun early when the Wassermann's reaction was negative without the reaction ever becoming positive. For this purpose easily absorbable preparations of mercury must be used, such as mercury salicylate, grey oil, and the like.

Although in a few cases it was possible by treatment to bring about a change in the reaction in congenital syphilis, most cases were extremely stubborn. Much more so was this the case in Syphilis hereditaria tarda. In only one case did a negative reaction result, but it required twelve courses to bring it about.

In late latent syphilis, of those which had been well treated 13 per cent. gave a positive reaction, those which had been insufficiently treated 36 per cent., those which had been untreated 81 per cent. Many of the cases in the tertiary stage were extremely difficult to influence by treatment. The author looks upon a positive Wassermann's reaction as being indicative of active syphilis, so that the patient should be treated until the reaction becomes negative.

J. McD.

A CASE OF LICHEN NITIDUS (PINKUS). Siegfried Reines. (*Med. Klin.*, 1910. Nr. 30.)

The patient whom Reines describes was a man, aged 30 years, who was admitted into the hospital on account of sexual neurasthenia. The skin of the scrotum and the penis was covered with several circular raised lesions, the size of a millet-seed; they were not follicular and they were not confluent, nor arranged in groups. The colour was the same as that of normal skin. Although the lesions were raised above the surface of the skin, the surface was inclined to be flat. Some of the lesions had a depression in the centre ("porus," after Pinkus). The lesions on the glans penis and the skin were smaller than those met with on the scrotum and flatter, and none had a central depression. The rest of the body was free. The localisation and character corresponds exactly to the Lichen nitidus of Pinkus. Clinically, there was no evidence of tuberculosis and there was neither a general nor a local reaction after tuberculin. Animal inoculation and auto-inoculation were negative after two months' observation. Histologically, the picture given represented the cases described by Pinkus and others, *i. e.* a collection of epithelioid cells with giant-cells situated directly under the epidermis and bounded laterally by a prolonged epithelial process. Surrounding the tubercle were mono- and polynuclear leucocytes. Caseation was absent. No tubercle bacilli were found.

A second case described by the author resembled that just related, and in both the prepuce was unaffected—a point upon which Pinkus laid emphasis.

J. McD.

THE EXPERIMENTAL PRODUCTION OF LEPROSY IN THE MONKEY (MACACUS RHESUS). Charles W. Duval. (*University of Pennsylvania Medical Bulletin*, p. 665.)

Many investigators have attempted to reproduce leprosy of man in the lower animal under natural and various artificial conditions, but aside from a slight local reaction that has occasionally developed at the site of inoculation the reported results have been invariably negative. Certainly there is no claim that the type of the disease as we see it in man has been produced under any conditions in the lower animal. Recently Clegg, Sugai, and the author, among others, have shown that leprous lesions occur in the guinea-pig, Japanese and white mice, following intra-peritoneal or subcutaneous injection of leprosy cultures. Three strains of *B. lepræ* were utilised in these experiments, one of which has been under cultivation for about a year and is now more than twenty generations removed from the parent stem, and the others have been growing upon artificial media six and nine months respectively.

On October 17th, 1910, a full-grown monkey (*Macacus rhesus*) was inoculated hypodermically into the subcutaneous tissues of the right inguinal region with 1 c.c. of a heavy homogeneous suspension of leprosy bacilli. Twenty-four hours after the injection the monkey appeared perfectly well and showed no signs of inflammation at the site of inoculation. Eight days later, October 25th, the animal was given a second injection of the culture into the subcutaneous tissues of the right breast. At this time there was still no evidence of either localised or general infection resulting from the first injection. The monkey was apparently in perfect health. One week after the second inoculation, or eighteen days after the first, a nodule the size of a split pea developed in the subcutis over the right groin at the site of the first inoculation, which slowly increased in size from day to day, and in three weeks attained the size of a pigeon's egg. At this time a small nodule also appeared at the site of the second inoculation. On November 1st the animal received a third injection of the culture into the subcutaneous tissue over the right groin, which was followed in forty-eight hours by the appearance of a hard nodular mass that has slowly continued to increase in size. The skin about this nodule shows numerous smaller indurated areas. The animal received a fourth injection of the culture into the subcutaneous tissue of the left breast on November 16th. In three days a purplish-red tumour, approximately 2 cm. in diameter, developed, and two weeks later the overlying skin became firmly adherent, thin, and shiny. The tumour mass ruptured on the seventeenth day, discharging a grumous material, which, on microscopic examination, contained large numbers of leproid cells filled with acid-fast bacilli. Cultures prepared from this material remained sterile with respect to pyogenic micro-organisms; however, *B. lepræ* was recovered in pure culture upon special artificial media.

Forty-six days after the first injection the monkey showed typical signs of disseminated infection, and presented the clinical picture of human leprosy of the tubercular type of the disease.

A successful experiment was also carried out on a second monkey. In the attempt to infect by way of the circulation, a third monkey (full-grown male) was given intra-venously into the left femoral vein a heavy homogeneous suspension of leprosy bacilli. The animal received in the same manner a second injection one week after the first, using twice the amount of culture as previously. At the present writing there is no evidence of cutaneous lesions or signs of infection elsewhere in the body. However, it is too early to expect skin-lesions at present. The successful transmissibility of leprosy to the monkey in all its clinical aspects clears up beyond doubt any question as to the identity of the acid-fast bacilli cultivated upon an artificial media from human leprous tissue, and proves conclusively that some strains, at least, retain their infectivity for more than a year under artificial growth conditions. These experiments also show the necessity of first cultivating the bacilli on an artificial medium in order to obtain large numbers of viable organisms if success is to be had in the experimental production of the disease.

J. L. B.

REVIEWS.

The Experimental Chemo-therapy of Spirilloses.*

This book represents the conclusion of studies which have been continued in the same direction for years, and have, in fact, occupied Ehrlich from the very beginning of his medical career. The result of these studies is little short of wonderful, and has roused the admiration of syphilologists all over the world, and raised hopes which bear every promise of fulfilment. In the introduction of "606" for the treatment of syphilis an undoubted advance has been made over all other methods of treatment, and to the perfection of the mode of application and the endeavour to increase the efficiency of the drug the attention of all who have to treat syphilis will be turned with the greatest enthusiasm. For it can hardly be hoped that a drug which will give even better results will be discovered during the next few years. We have for a long time had in mercury a specific remedy for syphilis, but a great disadvantage consists in its intense toxicity in relation to curative action. Therefore we cannot administer a dose which is sufficient to induce permanent cure within a short time, but, instead, the treatment must be carried out in stages. Mercurial combinations of less toxic nature have been employed, but even these have not entirely solved the problem.

The experimental treatment of the spirilla of syphilis was carried out on rabbits. Two forms of syphilitic disease can be induced experimentally in rabbits, namely: (1) Keratitis syphilitica, produced by the introduction of a small piece of diseased cornea into the anterior chamber of the observation

* *The Experimental Chemo-therapy of Spirilloses.* By Paul Ehrlich and S. Hata. Translated by Newbold and revised by Felkin. London: Rebman, 1911. Pp. 181. Price 12s. net.

animal. (2) Syphilis of the scrotum, produced by introduction of the inoculation material into a pocket in the skin of the scrotum.

Treatment of these animals with "606" showed that the spirilla can be destroyed absolutely and immediately by a single injection. With a dose of 0·015 grm. in two of the animals the spirilla were caused to disappear by the following day, while with a dose of 0·01 to 0·005 the spirilla were still present for two days in very small number. The cicatrisation of the chancre takes two to three weeks, but the disappearance of the spirilla is a far more certain indication of cure than the time taken for complete healing. The limits of the dose capable of immediate sterilisation lie between 0·015 and 0·01 per kilo. The minimum dose is 0·005 with which the spirilla can be destroyed within a few days, and with which, finally, definite cure can be obtained.

So much for rabbits. In man the strength of the dose has still to be determined. Local reaction phenomena not infrequently set in after the injection, and with small doses of poisons irritation is set up, the spirochætes are stimulated, and an increased production of poison takes place.

"606" is superior to mercury in the following conditions: (1) The cases with severe forms of ulcerating syphilis. (2) Malignant syphilis. (3) Cases with "psoriasis palmaris," with micro-papular syphilides. (4) Cases which cannot be influenced by Hg., and these include—(*a*) those which are altogether refractory to Hg.; (*b*) those which relapse shortly after Hg. treatment; (*c*) those which, despite Hg., relapse again and again; (*d*) those which possess an idiosyncrasy to Hg.

As regards the Wassermann reaction, it must be remembered that this reaction is positive in more than 50 per cent. of cases of syphilis treated with mercury for years, and it will be of interest finally to determine what this reaction shows under the influence of "606." This drug has great powers of cure in other spirillosis diseases, such as relapsing fever, framboesia, and spirillosis of fowls; also in trypanosome infections, such as sleeping-sickness, in malaria, and in variola.

In conclusion, Ehrlich believes that, seeing how thoroughly "606" has been studied both in man and animals, there is no urgent reason why our steps should be turned into a fresh direction, but, instead, that we may be perfectly satisfied with what we have attained up to the present. Such enthusiasm should arouse our admiration for the man, and what he has achieved we know.

J. L. B.

Techniques du Diagnostic par la Méthode de Deviation du Complément.*

Diagnosis by complement deviation now plays such an important part in laboratory work that this little book should prove very useful. To the dermatologist the estimation of the Wassermann reaction is constantly necessary, and it seems probable that in the future more will be done in the direction of the

* *Techniques du Diagnostic par la Méthode de Deviation du Complément.* By P. E. Armand-Delille. Paris: Masson. Pp. 200, 25 figures. Price 5 francs.

observation of complement deviation in tuberculosis, leprosy, sporotrichosis, and Mycosis fungoides. In the book before us the details of the preparation of the various elements—corpuscles, sera, antigens, and alexines—are described with great clearness and precision, and the descriptions are illustrated by photographs and diagrams, which considerably increase the usefulness of the work. The book should prove of service to the laboratory worker, and it is so clearly written that it should be read by any practitioner desiring information upon this valuable aid to diagnosis.

J. H. Sequeira.

Treatment of Syphilis by Salvarsan.*

Dr. Wechselmann was invited by Prof. Ehrlich to use salvarsan in his extensive service at the Rudolf Virchow Hospital so long ago as February, 1910. The work now translated by Dr. Wolbarst deals with the experience gained by the treatment of 1400 patients by the new remedy. Dr. Wechselmann gives a valuable account of the scientific and practical aspects of the use of salvarsan, and it is interesting to note that he, after trying both, does not think that the intra-venous method, in which he followed the technique of Schreiber, has any advantages over the subcutaneous injection of the neutral emulsion which he has so long practised. The question of the true value of the remedy is treated quite judicially, and Dr. Wechselmann insists upon the fact, so often forgotten by extremists both for and against salvarsan, that only after the lapse of years can the question of the permanency of the results be fully established. A survey of the German literature is given, and to this Dr. Wolbarst has added the reference to British and American papers. The work is beautifully illustrated by a series of coloured plates of cases before and after treatment.

J. H. Sequeira.

Skin-Diseases of Sexual Origin in Women.†

It is difficult to see the necessity for such a book as this. We have no idea for whom it is primarily written or to whom it is intended to appeal. To the dermatologist it can have but little interest, and the gynæcologist will not find much in it to help him, except a list of skin-diseases which have been described as occurring in pregnancy, diseases of the sexual organs, the climacterium, etc. A careful examination of these lists of skin-diseases will hardly convince him that they are always due to the abnormalities of the sexual organs with which they are associated. The dermatologist, moreover, may have still greater doubt on the subject; for instance, he may be sceptical as to an Alopecia areata being directly caused by pregnancy. Neither are some medico-legal questions satisfactorily solved by the author. Urticaria and Herpes zoster are, for instance,

* *Treatment of Syphilis by Salvarsan.* By Sanitatsrat Dr. W. Wechselmann. With an introduction by Prof. Paul Ehrlich. Only authorised translation by Abr. L. Wolbarst, M.D. Rebman, Ltd. 21s.

† *Hautkrankheiten Sexuellen Ursprungs Bei Frauen.* Oskar Scheuer. Berlin: Urban and Schwarzenberg, 1911. Pp. 203. Price 8 marks.

described as occurring in pregnancy, but the question of the justifiability of inducing abortion in such cases is hardly settled when we find that exactly these diseases are found in cases of castration in women. The question of the treatment of these skin-diseases is not touched upon, and this may perhaps induce the dermatologist to look with greater favour upon the book.

J. L. B.

Skin and Venereal Diseases.*

A summary of any branch of dermatological literature is now a formidable matter, so much has the literature increased within the last few years. In this book ten different authors have written monographs on special subjects under the editorship of Jesionek, and the magnitude of their work is shown by the literature of X-ray and radium therapy covering seventy-two pages, and that of eczema containing 1297 references and covering fifty-six pages. Both these subjects are dealt with in very considerable detail, and the author comes to the conclusion that the activity of radium is due to rays which have a very great similarity in their biological working to X-rays. A primary injury of the cells exposed to their action is followed by inflammatory phenomena; radium rays can further exert a retarding influence on embryonic development, while radium emanations can kill both frogs and white mice.

Jesionek has himself written an excellent article on the Wassermann reaction, in which he says that, although not perfect, and perhaps to be improved upon in the future, it is at the present moment the best indication as to whether a patient is suffering from syphilis. Treatment is to be begun as soon as a positive reaction is obtained, and only stopped when that reaction becomes and remains persistently negative. Some cases never show a negative reaction, either because they have not been treated, or have been imperfectly treated, and over these are always hovering the spectres of tabes and paralysis. Extreme caution is to be observed before assuring a patient that he is cured of syphilis. But if some years have elapsed since infection, the patient is in the best of health, and Wassermann reaction is constantly negative, such a favourable verdict may be returned. An excellent description is given in another section of the possibilities of preventing sexual diseases, but the cynic may, perhaps, be inclined to scoff at the efficacy of the proposed warnings to the public as to the dangers which they are running.

A good description is given of leukæmic diseases of the skin, but the literature is here not quite so satisfactory, and only two English references are given. Considerable space is given to the subject of gonorrhœa, but here the writer has not attempted the almost impossible task of coping with the literature of the subject.

We have no doubt that the book will prove of interest not only to dermatologists, but also to a number of practitioners who wish to keep themselves abreast of the latest advances in special subjects.

J. L. B.

* *Praktische Ergebnisse auf dem Gebiete der Haut- und Geschlechtskrankheiten.* By A. Jesionek. Wiesbaden: Bergmann, 1910. Pp. 573. Price 18 marks.

Beiträge zur Pathologie und Therapie der Syphilis.*

This volume provides a detailed account of the researches of Neisser and his collaborators on the pathology and therapeutics of syphilis. The greater part of the animal experiments were carried out in Sumatra (1905–1907), for which purpose an expedition was subsidised to the extent of 280,000 marks by the German Government. The discovery of the *Spirochæta pallida* just before the departure of the expedition no doubt acted as a great stimulus to the investigators. A glance at the contents page reveals the exhaustive nature of their researches.

Neisser himself is responsible for the first eleven sections. In these he treats of the disease in various monkeys with regard to incubation, distribution of the spirochætes in their tissues, infectivity of the internal organs, pathology of the disease, and resistance to re-inoculation. Neisser gives a detailed account of his views on the latter, views which are now held by the majority of workers on experimental syphilis. The "apparent immunity" to syphilis commonly observed is explained by the fact that the individual is syphilitic. The word "immunity," therefore, in this case is incorrect. An insusceptibility to super-infection exists, but only exists as long as the disease is present. In an animal which has become cured spontaneously or by treatment the insusceptibility to super-infection disappears, and it may be re-infected. The occurrence of a second infection of syphilis must, therefore, be taken as direct proof of the cure of the first infection. In his explanation of the above phenomenon, Neisser makes use of the terms "Anergie" and "Umstimmung." The insusceptibility to super-infection, *i. e.* "apparent immunity," he terms "Anergie." The partial insusceptibility observed in the incubation and early primary stages, as shown by the atypical primary lesions which result from a fresh inoculation of the virus, is the result of a modification of the living organism owing to the presence of spirochætes in the tissues. This altered susceptibility is in reality a manifestation of allergie, which itself is an immunity reaction.

The reactions of the tissues peculiar to the different stages of syphilis are explained on the hypothesis of "Umstimmung," literally a tuning of the tissues to respond in a certain manner. In the incubation period and primary stage of syphilis a lessened susceptibility to super-infection exists; this insusceptibility gradually increases till when the secondary stage is reached there is a complete insusceptibility, or, as Neisser calls it, "Anergie." This "Anergie" is regional in character, as it may be present in certain localities and absent in others in the same individual at the same moment.

Later, in the tertiary period, when the disease is less acute, "Anergie" has disappeared, though the tissues are still under the influence of "Umstimmung" from the spirochætes still in the system. A re-inoculation of syphilitic virus in this stage usually leads to the formation of a tertiary ulcer, a result which seems most likely to be a manifestation of allergie or anaphylaxis rather than a super-infection as some writers suggest. Neisser believes that the mechanism by which these factors are controlled is most likely to be of a cellular character, as up to the present no one has satisfactorily demonstrated specific immune

* *Beiträge zur Pathologie und Therapie der Syphilis.* By A. Neisser. Berlin: Springer, 1911. Pp. 624.

substances in the serum of a syphilitic patient or animal. In time, however, as more facts come to light, certain parts of Neisser's hypothesis must undergo modification.

The section on immunisation by Neisser and Bruck gave much valuable information concerning the above problem.

Neisser is also responsible for the chapter on therapeutics, in which research a large number of anti-syphilitic remedies, including many of the newer synthetic arsenical compounds, were tested as regards efficiency. The prophylactic value of many of these remedies was also investigated. The author believes that potassium iodide has some spirochæticidal power, and so advocates its use early in the infection. The section on the sero-diagnosis written by Bruck gives a full account of the history and technique of the Wassermann reaction. It has already been published by him at a date now somewhat past in monograph form.

The other sections are mainly concerned with syphilis in other animals (rabbit in particular), prophylactic experiments (Siebert), analogy between the Molluscum contagiosum of birds and syphilis from the point of view of immunity (Siebert), and vaccinia of apes (Halberstädter and Prowazek).

J. McI.

QUARTERLY SURVEY OF DERMATOLOGICAL LITERATURE.

ERYTHEMAS, INFLAMMATIONS, ETC.

Alopecia (Hypotrichosis) Congenita, Clinical and Experimental Observations on. A. Buschke. (*Archiv f. Derm. u. Syph.*, Bd. cviii, Heft 1 and 2, May, 1911, p. 27.)

Alopecia, Frequency of, at Different Ages. Sabouraud. (*Ann. de Derm. et de Syph.*, June, 1911, p. 349.)

Alopecics, Wassermann Reaction applied to. R. Sabouraud and A. Vernes. (*Ann. de Derm. et de Syph.*, May, 1911, p. 257.)

Comments on the Article, "A Comparative Study of Acrodermatitis Chronica Atrophicans and Diffuse Scleroderma with Associated Morphœa Atrophica," by F. P. Kanoky and R. L. Sutton (*Journ. of Cut. Dis.*, December, 1909). K. Herxheimer and Willy Schmidt. (*Journ. of Cut. Dis.*, xxix, May, 1911, p. 257.)

Dermatitis Repens and Acrodermatitis Perstans, A Comparative Study of. R. L. Sutton. (*Journ. of Cut. Dis.*, xxix, June, 1911, p. 325.)

Dermatoneuromyositis Chronica Atrophicans. A. Simonsohn. (*Archiv f. Derm. u. Syph.*, Bd. cviii, Heft 1 and 2, May, 1911, p. 59.)

Furuncle Treatment, The Collodion Ring. W. Fuchs. (*Münch. med. Wochenschr.*, May 30th, 1911, No. 22.)

Furunculosis. Shingleton Smith. (*Bristol Med.-Chir. Journ.*, June, 1911, p. 157.)

Furunculosis, Treatment of. F. Bruck. (*Münch. med. Wochenschr.*, June 20th, 1911, No. 25.)

Gangrene of the Skin. A Case of Idiopathic Symmetrical. E. Borzecki. (*Archiv f. Derm. u. Syph.*, Bd. cviii, Heft 1 and 2, May, 1911, p. 47.)

Granuloma Annulare (Radcliffe Crocker), to the Knowledge of. G. Arndt. (*Archiv f. Derm. u. Syph.*, Bd. cviii, Heft 1 and 2, May, 1911, p. 229.)

Helodermia Simplex et Annularis. H. Vörner. (*Archiv f. Derm. u. Syph.*, Bd. cviii, Heft 1 and 2, May, 1911, p. 161.)

Herpes Zoster, Two Cases in Conjunction with Kidney Disease. Rosenbaum. (*Deutsch. med. Wochenschr.*, June 15th, 1911, No. 24.)

Herpes Zoster and Renal Colic, Contribution to Knowledge of Head's Zones. A. Bittorf. (*Deutsch. med. Wochenschr.*, February 16th, 1911, No. 7, p. 291.)

Leucoderma in Burma. L. G. Fink. (*The Indian Med. Gaz.*, May, 1911, p. 176.)

Leucoplasia Præputis. Heller. (*Derm. Zeitschr.*, xviii, p. 666.)

Lichen Planus Bullosus, A Case of. J. W. Miller. (*Journ. of Cut. Dis.*, xxix, June, 1911, p. 332.)

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Lupus Erythematosus Linearis. R. Bernhardt. (*Archiv. f. Derm. u. Syph.*, Bd. cviii, Heft 1 and 2, May 1911, p. 55.)

Parapsoriasis en Gouttes to Brocq's Disease, On the Relation of. F. Heller. (*Archiv f. Derm. u. Syph.*, Bd. cviii, Heft 1 and 2, May, 1911, p. 71.)

Pemphigus, Ætiological Researches on Tropical. Bertarelli and Paramhos. (*Giorn. Ital. d. Mal. Ven. e della Pelle*, lii, Fasc. iii, 1911, p. 377.)

Psoriasis and Psoriasiform Syphilides, Diagnostic Value of Sero-reaction of Wassermann. B. Sabin. (*Ann. des Mal. Vénér.*, August, 1911, p. 594.)

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Urticaria Pigmentosa, On. Enzo Bizzozero. (*Ann. de Derm. et de Syph.*, July, 1911, p. 385.)

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Leprosy, A New View of its Bacteriology and Treatment. (Many illustrations.) T. S. Beauchamp Williams. (*Indian Med. Gaz. Supplement*, May, 1911.)

Leprosy, Present State of Our Knowledge of the Bacteriology and Ætiology of. E. J. Jeanselme. (*La Presse Médicale*, September 9th, 1911, No. 72, p. 721.)

Leprosy and the Question of Segregation, The Sociological Aspects of. Isadore Dyer. (*Journ. of Cut. Dis.*, vol. xxix, May 1911, p. 268.)

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Epithelioma of the Upper Lip in a Pure Negro. H. H. KERR and H. H. HAGEN. (*Journ. of Cut. Dis.*, xxix, June, 1911, p. 321.)

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Systemisation of Hyper- and De-pigmentation, A Contribution to the. Vörner. (*Derm. Zeitschr.*, xviii, p. 461.)

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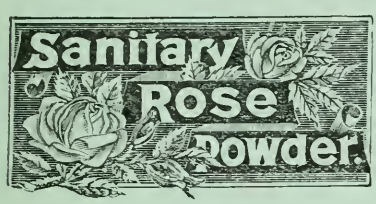

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